The Impact of Fetal Cardiac Intervention On Neonatal Cardiac Surgery

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• NO DISCLOSURES
Outline

• Overview of percutaneous fetal cardiac interventions
  – The case for fetal intervention (? altering the natural history of disease)
  – Case selection, timing
  – Team and equipment

• Complications

• Types of procedures
  – Aortic valvuloplasty
  – Atrial septoplasty
  – Pulmonary valvuloplasty
  – Fetal cardiac pacing

• The future
Non-Cardiac percutaneous Fetal Interventions

• Intrauterine blood transfusions for fetal anemia
• Insertions of pleural shunts
• Twin-twin transfusion syndrome: Laser photocoagulation of placental anastomoses to separate the circulation in monochorionic twins
• Bladder shunting
Fetal cardiac interventions

• Considered experimental by National Institute for Health and Clinical Excellence (http://www.nice.org.uk/IPG175)

• 4 main procedures:
  – Aortic valvuloplasty
    • Severe aortic stenosis with evolving hypoplastic left heart syndrome (HLHS)
  – Atrial septoplasty
    • HLHS with intact or restrictive atrial septum (PFO)
  – Pulmonary valvuloplasty
    • Pulmonary atresia with intact ventricular septum (Hypoplastic right heart syndrome)
  – Fetal cardiac pacing
The case for performing fetal cardiac interventions

- Surgeons have long argued that early neonatal repairs carried the promise of:
  - Improved ventricular function
  - Improved cerebral perfusion
The case for performing fetal cardiac interventions

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• Due to:
  -early removal of volume- or pressure-loading conditions on the ventricles
The case for performing fetal cardiac interventions

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  – Improved ventricular function
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Due to:
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Resulting in:
- early reverse remodeling due to neonatal tissues
The case for performing fetal cardiac interventions

• Therefore:
  – The reverse remodeling phenomenon should be even more pronounced in fetal life (and potentially allow for LV or RV “salvage”)

Aim of Fetal Cardiac Interventions

1) Promote ventricular growth and function
   - Univentricular $\rightarrow$ Biventricular circulation
   - Aortic stenosis with evolving HLHS
   - Pulmonary stenosis or atresia and evolving HRHS

2) Improve survival
   - HLHS with intact atrial septum
   - Salvage procedures (e.g. hydrops)
   - Fetal pacing for complete heart block?
Procedure

• Maternal general anesthesia
  – Uterine relaxation for fetal positioning

• Fetal intramuscular injection
  – Fentanyl Pavulon Atropine

• U/S guided needle access
  – Wire and balloon

• Access
  – Percutaneous
  – Laparotomy – transuterine

• Cardiac Puncture
  – Transplacental if needed
  – 19G solid stylet and cannula for cardiac puncture
Transuterine Technique – Fetal Aortic Valvuloplasty

UTERUS IS NOT OPENED
“Ideal Procedure”

• No hydrops

• Percutaneous

• Avoid placenta

• Two abdominal sticks
  – Fetal anesthesia
  – Cardiac access

• One cardiac puncture

• No fetal bradycardia, effusion or thrombus
Potential Complications

- Complications categorized as:
  - Fetal
    - Bradycardia
    - Pericardial and Pleural Effusion
    - Intracardiac Thrombus
  - Equipment related
    - Balloon rupture
  - Maternal
    - Surgical and Anesthesia
    - Obstetric
    - Prematurity
Potential Risk Factors

- Bradycardia
  - Gestational age
  - Procedure time
  - Hydrops
  - Laparotomy
  - Transplacental access
  - >1 cardiac puncture

- Fetal Demise or Prematurity + Death
  - Above variables
    - plus
    - Bradycardia

- Aortic regurgitation
  - Not considered a complication
  - Balloons intentionally oversized
Results – All Procedures

- Median GA: 24.4 weeks (20-34)
- Procedure time: 104 min (37-220)
- Hydrops prior to procedure: 15%
- Access via laparotomy: 28%
- Transplacental: 30%
- >2 abdominal punctures: 50%
- >1 cardiac puncture: 35%
<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia requiring Rx</td>
<td>30%</td>
</tr>
<tr>
<td>Pericardial effusion drainage</td>
<td>7%</td>
</tr>
<tr>
<td>Intracardiac “thrombus” (?)</td>
<td>15%</td>
</tr>
<tr>
<td>Fetal demise &lt; 72 h post</td>
<td>10%</td>
</tr>
<tr>
<td>(50% hydrops)</td>
<td></td>
</tr>
<tr>
<td>Premature delivery &lt;34w with death</td>
<td>5%</td>
</tr>
<tr>
<td>(1/2 prior hydrops)</td>
<td></td>
</tr>
<tr>
<td>Balloon Rupture</td>
<td>13%</td>
</tr>
</tbody>
</table>
Fetal Hemopericardium
Results – Maternal Complications

• No maternal deaths

• No anesthetic complications or transfusions

• Laparotomy wound infection 5%
  • Rx oral antibiotics

• Contractions requiring tocolysis 5%
Summary of Complications

• Procedural complications are common, especially with ventricular puncture

• Complications can be treated

• Fetal mortality
  – ~ 10%

• Premature delivery is uncommon but fetal hydrops is probably a risk factor for poor outcome
HLHS --- critical AS
Natural History of Fetal Aortic Stenosis

Typical Progression

22w Dilated LV

34w HLHS
Animal Models of Left Heart Hypoplasia
Increased LV Afterload

*Fishman et al. Circulation 1978;58:354*

Images courtesy of Abraham M. Rudolph, MD
Evolution of HLHS In Utero

In the fetus with evolving HLHS

- Can we promote a physiologic environment that facilitates normalization of LV growth and function sufficient to allow a healthy biventricular circulation?
  - How?
  - When?
Mechanical Regulation of LV Growth

Hypothesis:
• Blood flow stimulates cardiovascular growth in the fetus and neonate
• But how much do we really know?
  - Evidence is limited
  - Mechanisms not well characterized
Fetal Aortic Valvuloplasty Transuterine 20w

Needle to LV

Wire Across

Balloon Inflation
Acute Change in AoV Flow
23w - Post Aortic Valvuloplasty

AS jet 23 weeks
Pre valvuloplasty
~ 1mm jet width

AS jet 23 weeks
Post valvuloplasty
~ 2.5mm jet width
Fetal Aortic Regurgitation

- Intentionally over-sizing balloon
- Resolves within weeks (10/11)
- Well Tolerated
  - Low systemic resistance – placenta
  - High LV EDP
- Could there be beneficial effects?
  - Volume loading LV
Changes in Left Heart Size After Fetal Aortic Valvuloplasty
## Changes in Left Heart Function After Fetal Intervention


<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-dilation</th>
<th>Post-dilation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>23.5 2.1 wks</td>
<td>32.8 2.8 wks</td>
</tr>
<tr>
<td>Antegrade flow in TAA</td>
<td>(0%)</td>
<td>(69%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PFO bidirectional flow</td>
<td>(0%)</td>
<td>(25%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Biphasic MV inflow</td>
<td>(7%)</td>
<td>(93%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mod or severe MR</td>
<td>(54%)</td>
<td>(22%)</td>
<td>0.02</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>19 10</td>
<td>41 16</td>
<td>&lt;0.001</td>
</tr>
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Fetal Aortic Valvuloplasty for AS with Evolving HLHS 2000-2007

Procedures Attempted
N=57

Success
N=43

Failure
N=14

Technical Outcome

Pregnancy Outcome

Postnatal Outcome

Not Live Birth
N=5

Viable Live Birth
N=38

Not Live Birth
N=3

Viable Live Birth
N=11

HLHS*
N=27

2Ventricle Circulation
N=11

HLHS
N=11
Factors associated with a salvagable left heart remain to be determined
Staged Biventricular Reconstruction After Fetal intervention

Birth

After Biventricular Repair – 2 yrs age
Summary of Fetal Aortic Valvuloplasty

• Technical success: 80%
• Mod-severe AR post BD: 40%
• Technically successful aortic valvuloplasty:
  – Modest LV growth
  – Markedly improves left heart physiology
• Not a stand-alone intervention
• A subset of cases result in biventricular physiology
• It carries a risk of fetal demise (10%)
• Improved criteria for indication now available (multivariable threshold score)
HLHS with Restrictive or Intact Atrial Septum
• 18 patients (1990-1997)

• 6 survivors (33%) 

• All survivors had an unobstructed decompressing vein

• Standard HLHS stage I survival ~75%
Figure 2. Kaplan-Meier curves demonstrating estimated survival (freedom from death) over time among study patients born between 1990 and 1996 and those born between 1997 and 2002. Numbers of patients at risk are indicated below abscissa.
2001-2006
Children’s Hospital Boston

Graph showing the probability of survival over time since Stage 1 surgery (months).
Kaplan-Meier estimates of survival according to fetal intervention (p = 0.2)

Methods - Techniques

• Ultrasound guided

• 19G cannula with stylet and a 22G ultra-sharp Chiba needle

• 0.014” floppy wire and a 3 mm coronary balloon

• Procedural success
  – balloon inflation across the septum
  – improvement in color Doppler flow
HLHS Intact Atrial Septum
Fetal Stent Placement
Methods- HLHS with Restrictive or Intact Atrial Septum

Balloon Inflation     Flow Across Septum
Technical aspects

• More technically difficult
• Balloon dilation alone does not result in ASD that is large enough or stable enough
• Typically done in early-mid third trimester for technical reasons
• All neonate that had a >3mm ASD avoided invasive medical therapy and had more of a “typical” HLHS course
Pulmonary Atresia – Intact Ventricular Septum
Pulmonary Atresia with IVS
Outcomes After Fetal Diagnosis

Table 1: Fetal PA/IVS: Demographics and Post-Natal Outcomes, 1990-2004

- Fetal diagnosis PA/IVS: n=36
  - Live birth: n=25
    - Study group: n=23
    - Fetal intervention: n=2
      - Fontan: n=9
      - Glenn: n=5
    - Fetal demise: n=1
      - Termination: n=10
      - BTS: n=2
  - Non live birth: n=11
    - Biventricular repair: n=7

Salvin Abstract AHA
Fetal Pulmonary Valve Perforation and Dilation

• Only a few cases (11 in Boston)
• No major fetal or maternal complications
• midgestation
Limitations/Failures of Fetal Interventions

1) Technical Limitations
   • Fetal positioning
   • Fetal stabilization / movement
   • Imaging
   • Equipment inadequacies

2) Biological Limitations
   • No animal model
   • Late referral
   • Patient selection
   • Non uniform postnatal approach
What is The Impact of Fetal Cardiac Intervention On Neonatal Cardiac Surgery?

– fetal demise of 10%

– HLHS/critical AS:
  • marked impact on LV physiology
  • moderate impact on LV size
  • biventricular repair (25-30%) typically achieved at the cost of many surgical procedures

– HLHS/intact atrial septum:
  • marked impact on pulmonary physiology, ? pulmonary veins, ? outcomes
The Future

- Computer-assisted navigation (CANav) applied to fetal cardiac intervention

- The role of “open” fetal cardiac surgery vs fetoscopic cardiac surgery vs interventional remains to be defined
  (Ebsteins with hydrops; TOF/absent pulmonary valve)

- Where will we be in 20 years?